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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/067,094	02/04/2002	Om Reddy Gaddam	U 013821-9	5807

7590 04/07/2005

LADAS & PARRY
26 WEST 61ST STREET
NEW YORK, NY 10023

EXAMINER	
MCKENZIE, THOMAS C	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 04/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/067,094	GADDAM ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-65* is/are pending in the application.

4a) Of the above claim(s) *3-10,64 and 65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 11-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/4/04 & 7/27/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to amendments filed on 3/3/05. Applicant has not amended any claims. Applicant has canceled no claims. Claims 1, 2, and 11-63 were previously rejected. There are sixty-five claims pending and fifty-five under consideration. Claims 1, 2, and 11 are compound claims. Claims 12-23 are a composition claim. Claims 24-63 are method of using claims. This is the second action on the merits. The application concerns some α-ethoxybenzenepropanoic acid compounds, compositions, and uses thereof.

Response to Amendment

2. Applicants' new terminal disclaimers have been processed and overcome the two double patenting rejections made in points #11 and #12 of the previous office action.

Election/Restrictions

3. Claims 3-10, 64, and 65 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** effective traverse in the reply filed on 3/4/04.

Claim Objections

4. Objection remains to claims 20-23 under 37 CFR 1.75 as being a substantial duplicate of claims 12-15. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight

difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The phrase "for the treatment of type II diabetes ..." is a statement of intent. This is a purely mental act with no physical consequences. Thus, claim 20 is a composition claim with the same limitations as claim 12.

Applicants made no argument concerning this objection.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, and 12-63 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making solvates and polymorphs of the claimed compounds. The specification does not enable any person skilled in the art of synthetic organic chemistry to make the invention commensurate in scope with these claims. "The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or

unpredictability of the art, h) and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. In the present case the important factors leading to a conclusion of undue experimentation are the absence of any working example of a formed solvate or polymorph, the lack of predictability in the art, and the broad scope of the claims.

a) Determining if any particular substrate would form a solvate or hydrate would require synthesis of the substrate and subjecting it to recrystallization with a variety of solvents, temperatures, pressures, and humidity. The experimentation is potentially open-ended. Thus, the quantity of experimentation required is large. b) The direction concerning making the polymorphs is found on page 35, paragraph [000228]. The direction concerning making the solvates is found on page 35, paragraph [000230]. c) There is no working example of any hydrate or solvate formed. The claims are drawn to solvates, yet the numerous examples presented all failed to produce a solvate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ... no evidence that such compounds

even exist." The same circumstance appears to be true here. There is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, applicants must show that solvates can be made, or limit the claims accordingly. d) The nature of the invention is chemical synthesis, which involves chemical reactions.

e) The state of the art is that is not predictable whether solvates will form or what their composition will be. In the language of the physical chemist, a solvate of organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of West (Solid State Chemistry). The solvent molecule is a species introduced into the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West (Solid State Chemistry) says, "it is not usually possible to predict whether solid solutions will form, or if they do form what is their compositional extent". Thus, in the absence of experimentation one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometery of the formed solvate, i.e. if one, two, or a half a molecule of solvent added per molecule of host. In the same paragraph on page 365 West (Solid State Chemistry) explains that it is possible to make meta-stable non-equilibrium solvates, further clouding what Applicants mean by the word solvate. Compared with polymorphs, there is an

additional degree of freedom to solvates, which means a different solvent or even the moisture of the air that might change the stabile region of the solvate.

Joachim Ulrich, (Kirk-Othmer Encyclopedia of Chemical Technology) writes, "Pseudopolymorphs are solvates or in the case of water as solvent, hydrates, which means crystals that incorporate solvent molecules into the crystal lattice. Pseudopolymorphs exhibit different crystal forms and/or different densities, solubilities, dissolution rates, colors, hardnesses, etc. Compared with polymorphs, there is an additional degree of freedom (than temperature and pressure), which means a different solvent or even the moisture of the air that might change the stabile region of the pseudopolymorph." This means the stability of any particular solvate will depend on pressure, temperature, and humidity. Thus, solvates comprise an even less predictable art that other polymorphs.

The state of the art for making polymorphs is provided by Aronhime (Crystalline forms of pharmaceuticals and characterization thereof). Aronhime states on slide 4 that neither the properties nor the preparation of polymorphs are predictable. Aronhime (Crystalline forms of pharmaceuticals and characterization thereof) states on slide 4 that even the number of such polymorphs is unpredictable.

f) The artisan using Applicants invention to prepare the claimed compounds would be a process chemist or pilot plant operator with a BS degree in chemistry and several years of experience. g) Chemical reactions are well-known to be unpredictable, *In re Marzocchi*, 169 USPQ 367, *In re Fisher*, 166 USPQ 18. As discussed above, the art of solvate and polymorph synthesis is completely unpredictable. h) The breadth of the claims includes all of the hundreds of thousands of compounds of formula (I) as well as the presently unknown list of solvents embraced by the term "solvate". Thus, the scope is broad.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." After reconsideration of all the evidence, including Applicants' arguments, that conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Applicants point to paragraphs [000228] and [000230] as proving the guidance for the preparation of polymorphs and solvates respectively. Applicants then assert that the skilled chemist would be able to prepare both. The guidance in

the specification is of course, only one of the eight Wands factors, and not of the three the Examiner had considered as most important in the analysis of enablement. Presumably, Applicants do not dispute that the polymorph and solvate arts are unpredictable, that the scope of claims is broad, and there are no working examples of either solvates or polymorphs in the specification. Thus, the *prima facie* case of non-enablement has been made. According to MPEP §2106.02, " it must be emphasized that arguments of counsel alone cannot take the place of evidence in the record once an examiner has advanced a reasonable basis for questioning the disclosure. See *In re Budnick*, 537 F.2d at 538, 190 USPQ at 424; *In re Schulze*, 346 F.2d 600, 145 USPQ 716 (CCPA 1965); *In re Cole*, 326 F.2d 769, 140 USPQ 230 (CCPA 1964). For example, in a case where the record consisted substantially of arguments and opinions of applicant's attorney, the court indicated that factual affidavits could have provided important evidence on the issue of enablement. See *In re Knowlton*, 500 F.2d at 572, 183 USPQ at 37; *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979)."

6. Claims 24-63 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating type II diabetes, insulin resistance, and hypercholesteremia, does not reasonably provide enablement for treating the lengthy list of other claimed diseases. The specification does not

enable any physician skilled in the art of medicine, to make the invention commensurate in scope with these claims. The how to make requirement of the enablement statute, when applied to process claims, refers to operability and how to make the claimed process work. The factors to be considered in making an enablement rejection have been summarized above. The four main issues are the lack of any correlation between clinical efficacy for disease treatment and Applicants' one *in vitro* assay and two *in vivo* assays, the narrow scope of working data present, the state of the prior art, and the breadth of the claims.

a) Determining if any particular claimed compound would treat any particular claimed disease would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it clinical trials with a number of fundamentally different diseases described below, or to testing them in an assay known to be correlated to clinical efficacy of such treatment. This is a large quantity of experimentation. b) The direction concerning treating human diseases is found in paragraph [00016], spanning pages 7 to 8, which merely states Applicants' intention to do so. Applicants describe formulations in the passage spanning paragraph [000232], page 36 to paragraph [000240], page 39. Doses required to practice their invention are described in paragraph [000241], page 39. A 10,000-fold range of doses is recommended. Since no PPARγ receptor agonist

has ever been used to treat IBD, arteriosclerosis, and cancer, how is the skilled physician to know what dose to use for each of these different diseases?

There is an *in vitro* assay, drawn to hPPAR$_\gamma$, described in the passage spanning paragraph 449, page 98 to paragraph 451, page 99 with data on eight compounds. There is an *in vivo* assay, drawn to glucose reduction in mice, described in the passage spanning paragraph 453, page 100 to paragraph 458, page 101 with data on a single compound. There is an *in vivo* assay, drawn to cholesterol reduction in mice, described in the passage spanning paragraph 466, page 103 to paragraph 468, page 103 with data on seven compounds. Applicants do not state and it is not recognized in the pharmacological arts these three assays are correlated to clinical efficacy for the treatment of IBD, arteriosclerosis, and cancer, for example. There is a prophetic HMGCo enzyme assay and there are three prophetic diabetes, cholesterol lowering in the mouse, and obesity assays also described. None of Applicants compounds appear to have been tested for these therapeutic indications.

c) There is no working example of treatment of any disease in man or animals. There is no working example of any pharmaceutical formulation, which would be required by the physician to practice Applicants therapeutic claims. d)

The nature of the invention is clinical treatment of disease with agonists of the PPARγ receptor, which involves physiological activity.

e) The state of the clinical arts in PPARγ related diseases is provided by Cobb (Ann. Reports Med. Chem.) that antidiabeteic efficacy has been correlated to affinity to the PPARγ binding site, in the first paragraph, page 216. Sapone (Pharmacogenetics) reports that mice lacking any PPARα receptors develop normally. In his abstract he says that "[t]he biological significance of these novel PPARalpha alleles remains to be established".

f) The artisan using Applicants invention would be a physician with a MD degree and several years of experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), *Ex parte Sudilovsky* 21 USPQ2d 1702 (Appellant's

invention concerns pharmaceutical activity. Because there was no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) *In re Wright* 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain). h) The scope of the claims involves all of the thousands of compounds of claim 1 as well as the dozens of named diseases. Thus, the scope of claims is very broad.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Applicants dispute two of the eight *Wands* factors considered in an analysis of enablement and correctly state that some experimentation is allowed, if that experimentation is not undue. Applicants state that the skilled physician could consult books, journals, and presumably now the Internet, in order to practice the invention. Such a search would not reveal any successful clinical use of any

PPARγ agonist to treat any of the rejected diseases. Such a search would not reveal the dose of Applicants compounds required to treat any of the rejected diseases.

Applicants argue that no working example of a chemical invention is required for enablement and cite both *In re Stephens* 188 USPQ 659 and *In re Strahilevitz* 121 USPQ 561 in support of this assertion. This is not persuasive for three reasons. Firstly, while the present application is a chemical case, the claims presently rejected for lack of enablement are clinical claims not chemical claims. As reluctant as the Examiner is to admit it, the clinical arts are probably even more complex and less predictable than the chemical arts.

Secondly, *In re Stephens* 188 USPQ 659 concerned the manufacture of clay roof tiles. The court quoted with approval from the specification, that "the fired clay art is an extremely ancient one, and the production of fired clay roof tile extends back many years". In finding [1] the court concluded "[t]he specification proceeds to describe in considerable detail the individual steps and apparatus used in the process." Thus, *In re Stephens* 188 USPQ 659 is not on point technically because this was a mechanical not a chemical issue. *In re Stephens* 188 USPQ 659 is not on point legally, because the present case lacks in detail concerning the

claimed therapy and the use of PPARγ agonists clinically is so new that only diabetes treatment is an established use.

Thirdly, *In re Strahilevitz* 212 USPQ 561 concerned use of "a hapten-removing device" to achieve a therapeutic goal. Applicants' are claiming use of compound for achieving a therapeutic goal. The issue of the structure of the device was not directly considered by the court but it did note that in finding [3] that dialysis membranes were described in the specification and the court stated the "invention resides in combining the known prior art techniques of hemodialysis or hemoperfusion ...". One can infer the court believed the "a hapten-removing device" is a machine used for hemodialysis or hemoperfusion and was well known in the art. Thus, *In re Strahilevitz* 212 USPQ 561 is not on point technically because this was a mechanical not a chemical issue. Also Applicants are reminded that while the lack of any working example was not sufficient to establish the *prima facie* case of non-enablement, the courts held, "[h]owever, the examiner (and the board) also reasoned that enablement was not present because no dialysis or adsorption (of the antibody or antigen to the matrix) data were presented, and we are persuaded that this was sufficient to shift the burden to appellant to establish that a person of ordinary skill in the art could have practiced the invention

without undue experimentation." Thus, such a prima facie case had been established by the Examiner in *In re Strahilevitz* 212 USPQ 561.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

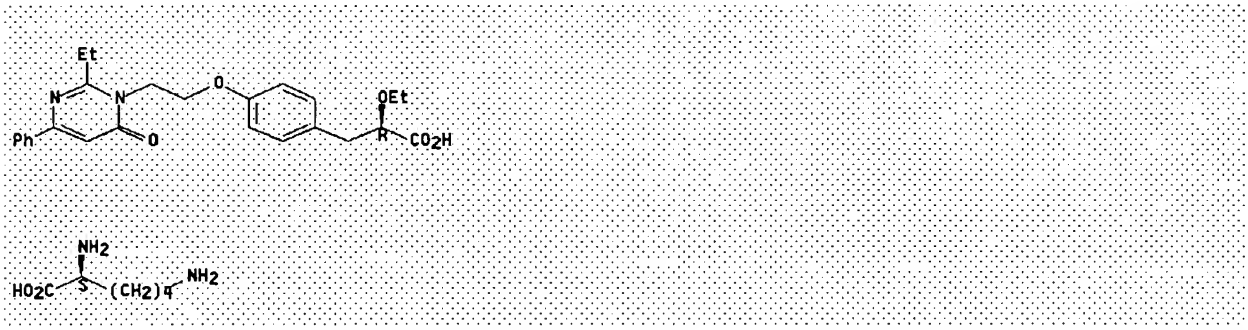
Claims 1, 2, 11-17, and 20-63 remain rejected under 35 U.S.C. 102(e) as being anticipated by Das ('816). The compound shown below fits formula (I) with M = K^+, R^1 = ethyl, R^2 = R^4 = methyl, and R^3 = propyl. It has Registry Number 446291-13-0 and is found in lines 11-16, column 85 of the reference. The compound is specifically named in the present claim 11. There are approximately 140 additional anticipatory salts found in this reference. Compositions are taught in claims 21, 32, and 34 of the reference. Thus, the present claims 12, 13, 20, and 21 are taught. Compositions containing HMG CoA reductase are taught in lines 35-45, column 34. Thus, the present claims 14, 15, 22, and 23 are taught. Claim 22 of the reference teaches tablets. Thus, the present claims 16 and 17 are taught. Treatment of hyperlipemia is taught in claims 24, 37, and 45 of the reference. Thus, the present claims 24-29 and 48-51 are taught. The treatment of both obesity

and cancer is taught in claims 24, 37, and 45 of the reference. Thus, the present claims 30-35 and 51-55 are taught. Treatment of Syndrome X is taught in claims 25, 38, and 46 of the reference. Thus, the present claims 36-41 and 56-59 are taught. Reducing serum cholesterol is taught in claims 26, 39, and 47 of the reference. Thus, the present claims 42-47 and 60-63 are taught.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

8. Claims 1, 2, 11-17, and 20-63 are rejected under 35 U.S.C. 102(e) as being anticipated by Gurram ('067). The compound shown below fits formula (I) with M = L-Lysine-H^+, $R^1 = R^3$ = ethyl, and R^4 = phenyl. It has Registry Number 408513-82-6 and is found in 16-22, column 59 of the reference. The compound is

specifically named in the present claim 11. There are approximately an additional 240 anticipatory salts in this reference.



Compositions are taught in claims 19, 21, 23, and 25 of the reference. Thus, the present claims 12, 13, 20, and 21 are taught. Compositions containing HMG CoA reductase are taught in the passage spanning line 57, column 37 to line 6, column 38, column 34. Thus, the present claims 14, 15, 22, and 23 are taught. Claims 20, 22, 24, and 26 of the reference teach tablets. Thus, the present claims 16 and 17 are taught. Treatment of hyperlipemia is taught in claims 28, 33, 37, 41, 45, 49, and 53 of the reference. Thus, the present claims 24-29 and 48-51 are taught. The treatment of both obesity and cancer is taught in claims 28, 33, 37, 41, 45, 49, and 53 of the reference. Thus, the present claims 30-35 and 51-55 are taught. Treatment of Syndrome X is taught in claims 29, 34, 38, 42, 46, 50, and 54 of the reference. Thus, the present claims 36-41 and 56-59 are taught. Reducing serum cholesterol is taught in claims 30, 35, 39, 43, 47, 51, and 55 of the reference. Thus, the present claims 42-47 and 60-63 are taught.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

These two anticipation rejections will be considered together. Applicants traverse these rejections and state that the terminal disclaimers overcome both. This is not persuasive. Only Applicant Paraselli is also listed as an inventor on the two prior art patents. The remaining five present applicants are not so listed. Thus, the two prior art patents are by another. Both prior art patent are assigned to Dr. Reddy's Research Foundation. The present application has no record of any assignment of right being made.

If the present application and the two prior art patents are commonly assigned, then the issue of priority under 35 U.S.C. 102(g) and possibly 35 U.S.C. 102(f) of this single invention must be resolved. Since the U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302), the

assignee is required to state which entity is the prior inventor of the conflicting subject matter. A terminal disclaimer has no effect in this situation since the basis for refusing more than one patent is priority of invention under 35 U.S.C. 102(f) or (g) and not an extension of monopoly.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 12-17, and 20-63 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Lohray (WO 99/8501 A2). The reference teaches the compound with registry number 220746-23-6 shown below. The Applicant claims the compounds M = Na^+, R^1 = ethyl, R^3 = hydrogen, R^4 = methyl, and an ethylene linker between the two rings. . The reference teaches a compound with a methylene linker between the two rings. The compound shown in the reference in lines 5-19, page 55. The difference between the claimed and taught compounds is the length of this linking carbon chain. It has been long established that a structural relationship varying the size of a linking carbon chain is *per se* obvious. Specifically, *In re Shetty*, 195 USPQ 753, *In re Wilder*, 195 USPQ 426 and *Ex*

Parte Greshem 121 USPQ 422 all feature a compound with a C_2-link rejected over a compound with a C_1 link. Similarly, *In re Chupp*, 2 USPQ 2nd 1437 and *In re Coes,* 81 USPQ 369 have a C_1 link unpatentable over a C_2 link. *Ex parte Ruddy* 121 USPQ 427 has a C_3 link unpatentable over a C_1 link. *Ex parte Nathan,* 121 USPQ 349 found the insertion of a C_2H_4 link obvious. In all of these cases, the variation was *per-se* obvious and did not require a specific teaching. In particular, the applicant is instructed to look to *In re Shetty*, 195 USPQ 753, *In re Wilder*, 195 USPQ 426 and *Ex Parte Greshem* 121 USPQ 422 where the deletion of one carbon atom of an ethylene functionality was found to be obvious over that of the prior art.

Claim 1 of the reference is drawn to "pharmaceutically acceptable salts". Compositions are taught in claim 25 of the reference. Thus, the present claims 12, 13, 20, and 21 are made obvious. Compositions containing HMG CoA reductase are taught in claims 46 and 52 of the reference. Thus, the present claims 14, 15, 22, and 23 are made obvious. Claim 26 of the reference teaches tablets. Thus, the present claims 16 and 17 are taught. Treatment of hyperlipemia is taught in claims

27, 31, 35, and 45 of the reference. Thus, the present claims 24-29 and 48-51 are taught. The treatment of both obesity and cancer is taught in claims 27, 31, 35, and 45 of the reference. Thus, the present claims 30-35 and 51-55 are made obvious. Treatment of Syndrome X is taught in claims 29, 32, 33, 39, and 42 of the reference. Thus, the present claims 36-41 and 56-59 are made obvious. Reducing serum cholesterol is taught in claims 30, 34, 37, 40, and 46 of the reference. Thus, the present claims 42-47 and 60-63 are made obvious.

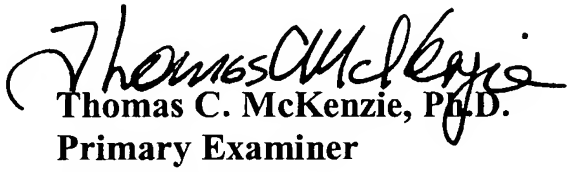
Applicants made no remarks concerning this rejection.

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Information regarding the status of an application should be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). Please direct general inquiries to the receptionist whose telephone number is (703) 308-1235.

12. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (571) 272-0670. The FAX number for amendments is (703) 872-9306. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, please contact Mukund Shah SPE of 1624 at (571)-272-0674.



Thomas C. McKenzie, Ph.D.
Primary Examiner
Art Unit 1624